UNITED STATES PUBLIC HEALTH SERVICE
RUPERT BLUE, SURGEON GENERAL

# YELLOW FEVER

## ITS EPIDEMIOLOGY, PREVENTION, AND CONTROL

(LECTURES DELIVERED AT THE UNITED STATES PUBLIC HEALTH SERVICE SCHOOL OF INSTRUCTION BY H. R. CARTER, SENIOR SURGEON UNITED STATES PUBLIC HEALTH SERVICE)

Lecture No. 1 (March 26, 1914)
Lecture No. 2 (March 27, 1914)

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# YELLOW FEVER.

## LECTURE NO. 1.

(March 26, 1914.)

I am directed to tell you something about yellow fever. In the time allotted it is impossible to cover the subject unless so superficially as to be useless to you. I am therefore going to take only one aspect of this disease, the one of most importance and of most interest to you.

You are, or ought to be, sanitarians, and it is the sanitary aspect of yellow fever only that I will present to you. I will not discuss the disease, as it concerns the practitioner. I am also going to assume a considerable knowledge of yellow fever in this class, because you have it. I am not going over a lot of facts well known about it, not because they are unimportant, but because you know them, and it would be a waste of time.

As a preliminary to the sanitation of any disease we must know its epidemiology, and to know this satisfactorily a knowledge of the method of its conveyance is necessary. Yellow fever, as you know, is one of the host-borne diseases. The history of the discovery and the demonstration of this by the Army board of which Maj. Reed was chairman are known to you. The subject is extremely interesting, but I have not time to go into it. The findings of the board were, briefly: *Yellow fever is contracted by man from the bite of a mosquito, itself infected by having previously bitten a man sick with that disease, and is only thus contracted.* The first part is a direct statement of observed facts, the latter a deduction (and a negative one) from the facts; both are not only universally admitted but abundantly proven, which is by no means the same thing. Upon this doctrine all sanitary measures for the control of yellow fever rest.

There are evidently three factors considered in the creed we have mentioned above—the sick man, the mosquito, the well man. There is also implied the infective microorganism of which as yet we know but little.

(1) You will find it very generally stated that the man is infective to the mosquito only during the first three days of his illness. This is probably true, yet I would like to give you the observations on which the statement rests.

Undoubtedly, all of the experimental cases were produced by mosquitoes which had bitten men during the first three days of illness. The reason was that the mosquito which infected the first experimental case was thus infected, and as the first experimenters were trying for positive results the conditions of the first successful experiments were copied. Other experiments followed them. Only a very few attempts then have been made to infect mosquitoes from men sick over three days. These few have failed. It is fair to say that a certain number of mosquitoes also failed to receive infection from man during the first three days. This would leave the matter in doubt.

The Pasteur commission, which studied yellow fever at Rio de Janeiro (Simon, Marchoux, and Salembeni), however, injected four men with the blood from yellow-fever patients in the fourth day of the disease with negative results. They had previously found this to be a very certain method of inducing the disease, more so than by mosquitoes. One of the men subjected to this experiment later developed yellow fever from the bites of infected mosquitoes. He then was susceptible to yellow fever. The commission regarded the others as susceptible also, but this was not proven.

Whether these four experiments, one of which only was on a man proven to be susceptible, can be accepted as proof that the blood of no man sick over three days is infective to mosquitoes, may be questioned. They are enough to render it probable, and we should be safe in saying that the blood is not infective after the first few days—three or four. At any rate I have given you the evidence as I recall it and you can judge for yourselves. I have not seen the report of the commission since it came out in 1903 or 1904, but I believe I have quoted it correctly.

(2) The only mosquito which has been proven to convey yellow fever is the *Aëdes calopus*, which was first known as *Stegomyia fasciata*, and then *Stegomyia calopus*. The cause of the change of name I do not know, but the Bureau of Entomology, which decides such matters, has so decided.

It is fair to say that not many experiments have been made with other mosquitoes. Only a few Culex, I think, have been tried and have proven negative. We can not, of course, accuse such mosquitoes as are found in any quantity where yellow fever does not spread. From analogy, not always a safe guide, we would suspect that some other species of this genus, or maybe subfamily, would convey yellow fever, and that none of any other subfamily would.

This is no mere matter of academical interest, but of practical importance. In Hawaii, for instance, a form known there as *Stegomyia scutellaris* exists in considerable numbers. If, as I suppose, it be of the same genus as the one which conveys yellow fever, which

used to be known as *Stegomyia calopus*, it is under suspicion as a breeder of yellow fever. On account of the position of these islands they will be exposed to the introduction of yellow fever when the Panama Canal opens, and mosquitoes which convey the disease must be eliminated. The breeding habits of the Scutellaris are not quite the same as those of the Calopus, and considerable extra expense is necessary if it also is to be eliminated. A British commission is about to study, or is now studying, the transmission of yellow fever by the scutellaris.

From the time the mosquito receives the infection from the sick man not less than 12 days must elapse before she becomes infective; that is, capable of conveying her infection to others. This period, of "extrinsic incubation" it was called when first discovered, is generally over 12 days, usually over 2 weeks, and varies with the temperature, being longer as the temperature falls.

It is somewhat strange that the only case in which this period has been found to be as short as 12 days was in the first case of experimentally induced yellow fever, that of Carroll.

When once rendered infective the mosquito remains so apparently all of her active life; in one of Reed's cases, 59 days after receiving infection.

Does she transmit this infection to her progeny? You know some hosts do. The cattle tick of Texas fever is a notable example. I think this is not true of yellow fever. It is true that Marchoux, of the Pasteur commission, working in Rio de Janeiro, reported such a case, but other attempts to do so have failed. Guiteras kept mosquitoes, the progeny of those that had transmitted yellow fever during the winter, and fed them from time to time on blood, some of the people furnishing it being susceptible to yellow fever. Rosenau, working at New Orleans and, I think, at Vera Cruz, also attempted to convey it from the progeny of infected insects and failed.

Naturally one positive experiment will outweigh a number of negative ones, but there are some things about the one observation of Marchoux that make one feel doubtful. "A light but undoubted case of yellow fever" he reported. It is sometimes not easy to be sure of one's diagnosis in light cases of yellow fever, and I wish he had not said "undoubted." I would not have used that word unless I had doubted it.

(3) The man who receives the infection. There is very little to say of him. The period of incubation in him is pretty accurately from three to six days. In 24 experimental cases and in 12 others where there was only a single exposure, the shortest time (one case only) was two hours less than three days. The longest time (one case only) was two hours more than six days. A number of cases

have been reported with shorter and longer, much longer, periods of incubation following the injection of blood or blood serum treated in various ways. This is not, however, the natural method of infection, and I think for practical work we should accept the period of incubation determined by infection received in the natural manner—by the mosquito. I need not tell you that the period of infection in man is of very great importance in the sanitary measures against yellow fever, especially those to prevent the introduction from one place to another, i. e., quarantine.

In all of this I have said no word of what is conveyed: What the mosquito takes from the sick man; what she imparts to the man who is susceptible to yellow fever; what produces the disease in him. And for good reason: I do not know what it is. Of course, since the disease is communicable, it is capable of self-multiplication, and hence caused by a living organism.

From the analogy with other diseases conveyed in similar manner the organism should be an animal parasite, a protozoan. It is a filterable virus passing through the Chamberland bougie. It is very fragile; heating to 55° C. destroys it. The blood remains infective a few days (five, I believe) under oil of vaseline, but soon loses this property if exposed to air. Many of us have attempted to cultivate this organism in various kinds of media without success; to find it in smears of blood; in sections of mosquitoes known to contain it; with various stains and differential stains; with dark field illumination; with ultra-microscopic apparatus. We tried in the laboratory on the Isthmus, but without success. Recently, about 16 months ago that is, Seidelin reported finding certain bodies, some in the red corpuscles and some in the blood serum, which he claimed to be the organisms causing yellow fever. I hope this is true, but so far his work has not been confirmed by others.

*The mosquito.*—Let us consider the mosquito that conveys this disease a little more in detail. Its name, genus, and species I have given you. It is a small, quick, very graceful mosquito; the day mosquito of the South. No one can mistake it. Once seen, both its appearance and feeding habits are distinctive. She is gray, and flies, as we say, "all adrift," with her legs spread out. Does not fly fast like the anopheline, but is quick in changing the direction of flight. She hovers before she bites, and as she bites, sings in a very annoying manner, and her bite is very irritating. She feeds in the daytime. I do not think the hour of the day has as much to do with it as the intensity of the light. On a dark day she will bite at noon, but generally bites from 3 or 4 o'clock to dusk and in early morning. She will bite, occasionally at least, in the night, but I do not think that she normally bites in the dark. It is a little hard to determine this by observation, and experiments, I think, have not been made.

How do you reconcile this with the belief that is so current in the South that one does not contract yellow fever in the daytime? I do not reconcile it. What I have said of her time of biting is true. I do not know that the other is. I do not believe it is. I have seen a great many places, small towns and places, holding "daylight communication" with places infected with yellow fever and believing themselves safe in so doing, but I have never yet failed to see these places receive infection if this was kept up long enough. It was always explained one way or the other. Some one had sneaked into the infected town at night, or had stayed after sundown, or some clothes had been brought from it, or something; but the fact remains that they received infection. It is claimed that people living in Petropolis are able to stay in Rio de Janeiro all day without contracting yellow fever, so long as they come out and sleep at Petropolis. It may be. I have no direct knowledge of the matter. The Pasteur commission, which accepts this, makes the hypothesis that while normal mosquitoes feed during the day, the infected ones must feed only between dusk and daylight. This is a deduction, however, and we have no observations to show it. In experimental work the infective mosquito feeds just as the uninfective ones do. This may not be conclusive, as in captivity they can not choose the time of getting blood, but I can cite one instance where those not in captivity did the same. In April, 1905, there was very little yellow fever in Panama. We had been nearly a month without a report of a case. In some way the executive building, where many clerks worked but which was not used for sleeping quarters, became infected, and we had, I think it was, 22 cases of fever contracted in this building within about 7 to 10 days. Now, this building was not open until 8 a. m. and closed at 5 p. m., and while some of the men may have worked after hours, none slept there, and the majority of those who developed fever kept the hours above given. They were unquestionably infected—that is, bitten by infected mosquitoes—during the day between 8 and 5.

This mosquito is domestic in her habits. She is found only about the habitations of man. She is not found in the marshes or the woods or fields. In the beginning of 1903 Manson, speaking of the introduction of yellow fever into the Far East by means of the proposed interoceanic canal, recommended that if such a canal were constructed it be deforested for a mile on either side to prevent the yellow-fever mosquitoes breeding there. In an article that I read before the public-health association that same fall the ground was taken that deforestation would be useless; that if protection from Stegomyia were needed depopulation of the canal banks would be far more efficient.

*Breeding places.*—By preference this mosquito is a "pot breeder." She lays her eggs in collections of clear—not necessarily clean—water in artificial containers, cisterns, tin cans, etc. I said "by preference." We find her breeding in other places, but generally where artificial containers are not available. I presume that when the necessity of ovi-position occurs she will deposit her eggs in the places of election if they are available, but if they are not available she will deposit them where she can. Therefore we occasionally have them in street gutters, and in pools in the earth. Probably a pool with clear water not disturbed, with firm earth sides, might do as well as an artificial container, but certainly she does not like muddy water.

*Distance of flight.*—It is a small, light mosquito and does not fly far from where she is brought to life. No direct experiments have been made, but the conveyance of yellow fever from an infected house is an indirect experiment, and I think it is fair to say that yellow fever will rarely be conveyed by mosquitoes 100 yards. White would put the limit far below this, but I believe that it is quite frequently conveyed by mosquitoes across the street or to a house back of the infected one. There are two cases, one reported by Melier and one by myself, in which it seems to have been conveyed much farther; in the first, 225 meters; in the second, 152 yards. Possibly we are both mistaken and there were some other means of infection than those we accused. Seventy-five yards would be about as far as you would expect it to be conveyed. This matter comes up in maritime quarantine as to how far you must lay ships off from an infected wharf. Quoting Goldberger I would say that "on account of its flight being only by day the direction of the wind during the day only need be considered in estimating this factor, if it be much of a factor, in their flight." Wind, I need not tell you, is generally onshore during the day—sea breeze.

*Distribution.*—It is a tropical or subtropical species, in the United States not found north of Norfolk or Virginia Beach. Some years ago I attempted to determine their presence in Baltimore by putting out breeding cans in a great many parts of the city and found this mosquito only at one point, the fruit wharf, where vessels from the banana ports came in. The old quarantine division making the southern boundary of Maryland the division between "infectible" and "noninfectible territory" seems to be justified.

In the tropical and subtropical belt it is found in practically all of the hot, wet countries; at least on the seacoast. This is doubtless due to its ready conveyance by vessels. Fortunately, although the mosquito is distributed so very widely, the parasite, the carrying of which makes it so dangerous, has by no means had so wide a distribution.

*Conveyance.*—It is conveyed by vessels almost any distance. The old sailing vessels were really hosts to it, as this mosquito bred in their water tanks without limit as to either time or distance. Steam vessels carry it much less, as they have far fewer collections of water accessible to mosquitoes aboard. They probably rarely breed on such vessels, but may travel as mosquito imagos for many days.

Are they conveyed in railroad coaches? White, who has studied the subject, thinks not. They were reported to me as found only in a single instance (Evansville, Ind.) in Pullman cars in 1903. But the fact of the development of yellow fever at Bristol, Tenn., at Louisville, and at St. Louis in 1878 among railroad men employed at these stations and who contracted it about these stations, I think, can be explained only by the fact of these mosquitoes being carried by railroad coaches. Occasionally I would say, then, that they are, but that is not common.

They live a long time; one in captivity—an infected one—was kept by Guiteras five months.

*Hibernation.*—How do they live during the winter? Their eggs are quite frequently laid above water, and these have been known to retain their vitality for over two months and a half. Possibly this may be a method. The imagos unquestionably hibernate in the Gulf States, and may do so farther north. Guiteras kept a number without food or water in a refrigerator for three months, when they were eaten by ants. There is no question that the species hibernates as far north as Norfolk and that the imagos hibernate on the Gulf coast. I have seen them in February and March.

Do the parasites hibernate in their hosts? I think not. I have done a good deal of postepidemic disinfecting and have advocated it, but I think I was wrong; that the work was useless at least in the United States.

It is claimed that two, possibly three, epidemics in New Orleans arose from infection left the previous year, but it is certain that none has so started in Mobile, nor in the little towns along the Gulf coast, in Pensacola, nor in any of the towns of the Atlantic coast from Jacksonville to Norfolk, and generally it has not been the case with New Orleans. Now numbers of these mosquitoes must live through the winter and numbers of them must have been infected when hibernation was begun; if then they do not convey infection the next year, the parasites in them must have died. It was on this account I said that once infective the mosquito remained so during her *active* life. Infection apparently dies out during hibernation. Possibly infected females may not hibernate. The general experience of yellow fever not recrudescing the year after an epidemic is proof that generally the parasites die. The negative evidence is so strong that it seems fair to believe that the fever alleged to have been "kept

over" in New Orleans was an introduction early in the season, the source of which was not known. It is a matter that could be easily settled by laboratory experiment, and, if I am correct, with no danger to the men subjected to it.

### The Sanitation of Yellow Fever.

I think I have said enough to enable you to appreciate the sanitary measures to be taken against yellow fever.

First. To prevent its introduction into places where none exists. If there be no *Aëdes* (*Stegomyia*) *calopus* in the places to be protected they need no protection, as it is "uninfectible territory" in which yellow fever is not a communicable disease. You may introduce a hundred cases in the absence of the mosquito and there would never be one hundred and one. This is true of the ports of the United States from Baltimore north. It is the meaning of the old division line between "infectible" and "noninfectible" ports.

Of course the same thing holds when the mosquitoes are inactive; that is, even at southern ports during the winter. Cases of yellow fever introduced then have nothing to be infected by them. Infected mosquitoes even would not be able to leave the vessels. Quarantine is properly modified then by the condition of the port to be protected as much as the port to be quarantined against, a thing which more than once has been overlooked. And here let me warn you against unnecessary measures of sanitation. They bring reproach upon the whole subject, and being indefensible, render it less easy to defend the necessary measures; moreover, there is only a certain amount of money, time, and energy available for sanitary measures, and as in old times the tithing of mint, anise, and cummin leads to the neglect of the weightier matters of the law. It is very important, then, to take no unnecessary sanitary measures.

Second. To eliminate yellow fever where it exists. I say eliminate, not control. The latter is allowable for malaria, but I think that for yellow fever the sanitarian should be satisfied with nothing short of elimination. It is easy.

Since two hosts, one human and one insect, are necessary for the propagation of yellow fever it is obvious that a perfect control of either is sufficient for the elimination of this disease from a community. I mean that if every person developing yellow fever was immediately isolated from these Aëdes mosquitoes (that is, if no access to him by mosquitoes was allowed while he was in an infective stage) yellow fever would inevitably cease. Similarly, if there was no access to man (I mean man susceptible to yellow fever) by any mosquito in the infective stage, the same thing would occur. Theoretically, then, we can eliminate yellow fever by control of either the human or the insect end of the chain.

At which end of the chain shall we begin? Shall both ends be tried at the same time? One method is not incompatible with the other.

At first sight it seems most feasible to try to control the human host, because, (1) we can tell more or less when he develops yellow fever; (2) when found we can isolate him by wire screening or otherwise from mosquitoes; (3) *the period of infectivity of the human host to mosquitoes is very short*, three or four days at most, *during which time only* he need be guarded.

On the other hand, these mosquitoes once infective remain so indefinitely, and, except as their environment creates a presumption that they have or have not had access to a man in the infective stage of yellow fever, we have no means of telling infective mosquitoes from any other, and the only practicable means of control of the insect host is by its extermination—more or less complete.

The destruction of the *Aëdes calopus* mosquitoes, which have had access to a man in the infective stage of yellow fever, as distinguished from the general destruction of these mosquitoes, requires such a knowledge, and hence control, of the human host as to place this measure in the class of those determined by the control of the human rather than in that of those determined by the control of the insect host.

It seems easier, then, and more natural to attempt to control the human host; and the first attempt to exterminate yellow fever after its method of propagation was known, which was so brilliantly carried out by Gorgas, at Habana, in 1901, rested mainly on this method. The attempt to lessen the number of mosquitoes by destroying their breeding places was also made, and made vigorously, but the principal dependence was placed on the isolation of the infected men, and the destruction of the mosquitoes already infected by them; the destruction of *Aëdes calopus* in general being regarded as an adjuvant to the main work.

The same methods were used by Liceaga, for Vera Cruz; by Oswaldo Cruz, for Rio and Para; by White, for New Orleans; and finally by Gorgas, for Panama and Colon. Its general adoption, then, shows this to be the most natural method.

All of these efforts were successful, or comparatively successful, those in Habana and on the Isthmus especially, and that in Habana brilliantly so. Yet Col. Gorgas believes and asserts that his success in Habana was due to the war waged on the mosquito, directly undertaken as an adjuvant to the isolation of the sick, rather than to that isolation itself; to the control of the insect rather than to the control of the human host. This certainly was the case in the Isthmian work. He controlled the fever by the isolation of sick men, and greatly lessened its spread, and would bring it down to the very few cases per

week or even per month. But it seemed that it would not disappear, no matter how closely this work was done, and I can not assure you that it was done very closely. I do not know of any higher praise that I can give Col. Gorgas as a tactician than to tell you how he pressed home the flank attack, so to speak, when we found that the main effort was not going to be successful.

The reason that the method by control of the human host failed was because under the conditions that existed it was impossible to carry it out. We could not control the human host to the degree necessary for success. No one who has not conducted a campaign against yellow fever in a place where it is endemic, where the inhabitants do not fear it, can imagine the difficulties of finding the cases of yellow fever early in the disease, or at all; even the cases which are plain. For the light cases let me say this: An analysis of the yellow-fever statistics of Habana for the 10 years preceding 1895, published by me in 1900 in the United States Public Health Reports, led me to state that but a small proportion of the cases of yellow fever in Spanish adults in Habana, about one-eighth, I think, had been diagnosticated. Taking this into account, in addition to the cases in native children, which are practically never diagnosticated, I think the most optimistic will admit that in such places control of the human host to a sufficient degree to eliminate yellow fever is impossible—not difficult, but impossible. Our only hope, then, is to control the insect host, to destroy the *Aëdes calopus* mosquito.

This is true for towns where yellow fever is endemic. In towns where it is not endemic, as in the United States, the conditions are different. With the cooperation of the people it is or may be possible to control the human host sufficiently in such a town, especially if the town be small, or, what is nearly the same thing, if the fever be confined to a limited area in a large one. This was, I think, an important factor in the success of White's campaign in New Orleans. Although the elimination of the breeding places of these mosquitoes was pressed most vigorously the results were too quick, I think, to be due to their extermination by this method. Certainly the early control—I do not say elimination—of the fever was due to this. This was the method used successfully in the suppression of an epidemic in the little town of McHenry, in 1898, I believe, and in Hampton, Va., the next year by White and von Ezdorf. The method of conveyance of yellow fever was not known at that time and the attempts were naturally made entirely from the human end of the chain. They were successful.

In towns in the United States, then, when the people will cooperate, attempts to control the human host must always be made, for they will control the fever even if they do not eliminate it; they

will smother it; lessen its rapidity of spread so that we can tide over the time until frost with a minimum number of cases. We have no frost to help us where the fever is endemic. This was the case in the little town of Franklin, La., in 1897. The fever was handled by isolation and fumigation with sulphur of the houses in which it occurred. It spread very slowly and we had only 10 or a dozen cases from September 1 until frost, which came on the night of November 18—plenty of time for a full sized epidemic, but for the measures taken.

Since the essential part of this method is the discovery of the man as soon as he is sick, the cooperation of the town people is necessary. Light cases are far more readily found in such towns than where the disease is endemic because, as a rule, the whole population is susceptible to yellow fever, and a light case of one member of a family is very apt to be associated with clearly marked cases of some others in the same house and thus lead to discovery or at least suspicion.

On the other hand were the problem to rid of yellow fever a town in the Tropics in which it is endemic, as, say, Guayaquil, I would concentrate all my energy in ridding the town of *Aëdes calopus;* I would not isolate those sick of yellow fever; I would not isolate a man; I would not fumigate a room save possibly as a protection to those in the immediate neighborhood. As a measure of general sanitation helping to rid the town of yellow fever its value would not pay for the trouble it causes if indeed it had any value at all for this purpose.

The conditions of the two classes of places are different and the means advisable for the riddance of yellow fever are also different. For the last, control of the insect host alone is to be aimed at; for the first, control of the human host should also be vigorously pressed.

One does not have to eliminate all the *Aëdes calopus* to get rid of yellow fever; if they are brought to below a certain number in a town, the disease will spontaneously die out. This is common sense rather than observation, and the number necessary to continue it should vary directly with the ratio of people immune to yellow fever to those susceptible to it. Thus, suppose 10 cases of yellow fever were introduced into a town all of whose inhabitants were susceptible to the disease; suppose, then, that there were such a number of these mosquitoes in the town as were able to infect only 9 men from these 10 sick ones, obviously the fever would gradually die out. If there were enough to infect 11 men, it would increase. If the number was such that they were just able to produce 10 infections, the fever would continue without increasing or diminishing. Now, if one-half of the people in the town were immune to yellow fever, obviously

only 5 infections would be caused by this same number of mosquitoes—one-half of their bites being wasted on those immune to yellow fever—and there would have to be twice as many to be able just to continue the fever. Obviously, then, the "critical number" of Stegomyia (as Gorgas calls the number just less than which will allow yellow fever to spread in a town), this "critical number," I say, is less in any town as the number of those immune to yellow fever decrease, and a much greater mosquito reduction is required to eliminate yellow fever from a town in the United States, where practically all are susceptible to yellow fever, than from one where it is endemic. Therefore, it is far more difficult, the work must be carried further, to eliminate yellow fever in a town of the United States than in one where it is endemic. I had rather tackle three towns like Guayaquil than one like New Orleans in 1905.

There is one other thing that is not yet in the books and yet that is fairly well known by sanitarians and which you should know. It is the spontaneous disappearance of yellow fever in towns in the Tropics. There are quite a number of towns of this kind from which yellow fever has disappeared where no sanitary work has been done and which are still breeding Aëdes, or before sanitary work was done. Corinto was unquestionably infected with yellow fever in 1905. We had an inspector there until 1910 or 1911. No sanitary work was done and *Aëdes calopus* was breeding all of this time, yet in 1911 or 1912 we landed some 5,000 marines, who made the place the base of operations and stayed there some time. No fever appeared among them. Evidently the town was not infected. Bocas is free and no sanitation was done until after the fever was gone. I think the same thing happened in some of the towns in the interior of Cuba, as Puerto Principe and Villa Clara and even Cienfuegos. It has been a not uncommon phenomenon in the Tropics. Yet most of these towns—I except the Cuban towns—are still breeding *Aëdes calopus*. How does this happen? Unquestionably by the elimination of the parasite, by the failure of the human hosts in sufficient number to continue its propagation. If all the people in an endemic center become immune and no nonimmunes come in, there is nothing to keep up the human chain, and when the infected mosquitoes die out, if they have not bitten some one who can continue the propagation, yellow fever necessarily stops. It is a spontaneous elimination of the parasite for the lack of a human host. This does not occur in large towns. Too many immigrants come in from places where yellow fever is not endemic and the infection is thus kept up. There are also a larger number of babies born, who, of course, are newcomers and susceptible to the disease. I will say this, however, that it would require a decidedly larger number of babies per annum to continue the propagation of yellow fever than it would of sus-

ceptible people from the outside. When yellow fever is getting rare in a town a baby remaining in its own home would be far less exposed to it than an adult going from place to place in the town. A baby while sick would be in the house of its immune parents and would thus have less chance to spread it than an adult who would contract the disease in one part of the town and develop it in another. On both counts, then, a baby is less apt to propagate it than a susceptible adult.

One thing is also to be noted, that towns of this kind are liable to little epidemics among the natives from time to time when yellow fever is introduced. This is due, of course, to the accumulation of a considerable number of people susceptible to the fever; that is, to those born since the town was free from infection. There was one at Buenaventura in 1904.

## LECTURE NO. 2.

(March 27, 1914.)

GENTLEMEN: I told you yesterday something of the epidemiology of yellow fever—enough to understand the reason for the sanitary measures to be taken to control it. I also discussed the class, the general nature, of these measures. I thought that to-day I would take up the sanitary measures somewhat in detail, not simply giving you the principles upon which they are based nor the general direction in which they should go, but the details of sanitary measures.

There are two lines along which efforts to eliminate yellow fever from a place may be made. One is by the control of the human host and the other is by the control of the mosquito. There are good reasons why in a large place where yellow fever is endemic the attempt to eliminate it by the control of the human host is futile.

I should like to tell you what was done in Panama. I do not know that anything could give you a better illustration of sanitary tactics than what occurred when we found the attempt to control the human host had failed and the attack against the mosquito was pressed to success. I want to take up these two lines now in some detail.

What measures do you take to eliminate the insect host or, I will say, to control the insect host? Here we encounter the same difficulty that we find when we attempt to eliminate other things that breed very fast, such as rats, mice, flies, fleas, etc. There is no use in attempting to destroy the individual. This does only temporary good, and only a little good after all. You will never be able thus to get rid of them. The only chance of success is in destroying their breeding places, their shelters, their food supplies, or of introducing such natural enemies as may be able to keep them under control.

This mosquito's food supply is man—ourselves; their shelters are our houses. No natural enemies have been found which will control them. We must necessarily limit our campaign to an attack on their breeding places. Fortunately this is easy. In attacking their breeding places we have only to get rid of water in artificial containers or to prevent access of mosquitoes thereto. There is no problem here of draining measures, draining streams and swamps and cleaning out ditches, as we have to do in antimalarial work. If we eliminate the artificial containers about the houses of man we practically get rid of the yellow-fever mosquito and consequently of yellow fever itself. I may say that they were reported breeding in the street ditches in

New Orleans on the outskirts of the city in 8 per cent of the ditches. This certainly was not so, however, in Habana or in Panama; and I am informed by Richardson and White that the determination of the species found in the ditches in New Orleans was made almost exclusively from the larvæ, by whom I do not know, and it is very easy to make a mistake between the larva of the Culex and the *Aëdes calopus*. At any rate, in Panama, Colon, and Habana we did not find *Aëdes calopus* breeding in street ditches as a sanitary problem. It was entirely a question of artificial containers.

Of course, if there is a mudhole or a ditch with firm sides containing clear water, I do not know but that it might not do as well as an artificial container and that these mosquitoes might not breed there just as well as in a jar. But the fact remains that we rarely, if ever, find this mosquito in puddles or ditches.

You must not leave artificial water containers anywhere about the premises. Cisterns and water barrels are the main breeding places, but by no means all. At Colon there was a very excellent officer as superintendent of the hospital. I was over one day to see a case of yellow fever and while there I thought I would look around to see whether there were any breeding places for mosquitoes. He laughed and said there were none. "I knew you were coming," he said, "and cleaned up everything." I did not find anything except about a pint and a half of water in a grindstone basin, and if there was one there were a million larvæ in it. He had not thought of that. In the executive building in Panama mosquitoes were found breeding in the dishes where the brushes for the copy books were kept. In a little office where there were three or four desks in Gen. Wood's headquarters in Habana they were found breeding in fire pails, and in some houses rather carefully inspected they were found breeding in the little saucers in which table legs were set to keep the ants off the table. There is not any collection of water too small for these mosquitoes to breed there and in numbers. We found them in the holy-water basins in the cathedral and experienced a great deal of trouble in getting rid of them.

Another thing: The gutters of buildings had to be looked after pretty closely. If they were crushed or bent they held water; if they were stopped up with leaves or trash they held water. I thought where there was just a slight sagging, a bit holding a few ounces of water, with a pouring rain averaging twice a day, there would be very little risk of *Aëdes calopus* breeding there; but the last mosquito work in Panama was done to remedy just that condition in the gutters.

I found a child with yellow fever at the Hotel Italia and I found *Aëdes calopus* in the room where the child was sick. Where did

they come from? I naturally thought of the cistern as not being screened. I went out and examined it and found it well screened. It was tight. But we opened the cistern and one or two of these mosquitoes flew out. I got down in the cistern (it was an underground affair in the kitchen) and found a few larvæ on the surface, but there were many pupæ skins scattered about. I was puzzled to know how the mosquitoes got into the cistern, which was, as I said, tightly screened. Then it flashed on me all at once that while the screen through which the water poured into the cistern at the intake was fine enough to screen out the mosquitoes; it was not fine enough to prevent the eggs and the very young larvæ from the gutters from washing down into the cistern. In that way they would develop just as well and come out of the cistern as they would if they had been laid directly in the cistern water. To correct the condition we did two things: We set the tops of the cisterns on permanently with cement and put in pumps, so that if mosquitoes developed in them they could not get out, and later discontinued cisterns altogether.

That is a thing you will have to watch for if you have any work to do in the extermination of mosquitoes. You had better not have gutters on the houses, but if you have gutters let them, as a rule, be not over 16 feet long, with a down spout at each end discharging on the ground. Do not use any cisterns if avoidable.

You need not pay any attention to open cesspools. You may have as many cesspools as you choose. These will breed Culex, but you will never find *Aëdes calopus* coming out of a cesspool. The *Aëdes calopus* does not like that kind of water; she requires clear water to breed in.

Another thing: How about the cups provided by the leaves and branches of plants? This may be matter for important decision sometimes. There are a number of plants that hold a little water in the axils of their leaves. A cornstalk does; so does the caladium which adorns our lawns. In the Tropics you will find plants that will hold some ounces of water, or even half a pint, and these may furnish breeding places for our mosquitoes, because the water is clear. The banana and taro (colocasia) should be especially noted, as the axils of their leaves may hold considerable water. The leaves of certain palms also form cups that hold water; some, as the coconut palms, very little, while the Traveler's palm will hold, maybe, half a pint. The colocasia, however, was our main concern on the Isthmus, as they were all around the houses and held two ounces of water or more to the plant. In this water the larvæ of *Aëdes calopus* was sometimes found, usually, however, in small numbers.

As I told you, I think, a mosquito lays by preference where her progeny is most apt to come to maturity, but she will lay by obliga-

tion wherever there is water when she can not find a better place, as she can not help laying any more than any other female animal can.

To determine, then, if the water in these colocasia plants was suitable to bring the larvæ to maturity we put screens of wire or of hoops and mosquito netting (just the arrangement one uses to keep flies from cake) over these plants where there were collections of larvæ, and from what I saw I do not think 5 per cent of them developed into mosquitoes.

Bananas were examined and were not considered dangerous. I do not recall whether no larvæ, or very few, were found in them. These plants are not plentiful about the city of Panama. I do not know that any palms were examined. I think we had only two Traveler's palms on the Isthmus, and we did not fear the others. On the Isthmus, then, we did not consider the breeding in the axils of leaves of plants of sufficient sanitary importance to take measures against it. I can conceive, however, that the Traveler's palm may be a decided danger; as, indeed, under different conditions, the other plants mentioned might be. I am only telling you what the conditions were on the Isthmus; they might well be different elsewhere. It is fair to say, too, that on the Isthmus the removal of "cover" for mosquitoes in the neighborhood of houses removed most of these plants any way.

What I want you to notice here is not that we considered the breeding in plants of little sanitary importance, but the method of determining that it was not. To find larvæ in a collection of water is not proof that this collection is breeding. See if they develop into imagines before you say that.

Aëdes do breed in knot holes in trees. At Corinto the knot holes and hollows in the firewood which was piled on the wharf was a source which had to be reckoned with.

In artificial containers there are three methods you may adopt to get rid of mosquito larvæ or eggs: Turn the water out; screen the container; or, if these two are impracticable or not permissible, oil the container. This seems a simple thing to tell you, but it is a point you may have occasion sometime to remember. In turning the water out of the container turn it completely out; do not leave any water in it, or you will have to do your work over again. This mosquito has probably been turned out of water jars for generations. Those that have been turned out have not bred any progeny, and only the progeny of those that knew how to take care of themselves are alive. Thus the instinct to save themselves is strong in them now, and I must say that a great many of them seem to know how to take care of themselves. For example, of 100 larvæ in a jar that has been turned out, if you leave 50 drops of water in the jar you will find 99 of the original larvæ in the bottom; and the only way to make a

good job of it is to turn it completely upside down and get rid of every drop of water that is in it. They cling to the last few drops of water left in the jar.

As to oiling containers, that, of course, can be done only when the water is not to be used for drinking or cooking purposes and where you can not turn it out. You will find this to be the only method available in a great many places. Salt, if enough be added, will also prevent breeding. This was the means used to get rid of them in water about a church which could not be oiled.

There is one thing you will have to bear in mind: If you turn a water supply out you have got to furnish other water for it, and this is not always easy to do. Supplies of wholesome water are often scarce, and in places where yellow fever is epidemic waterworks are usually conspicuous by their absence. In such places a man often has to buy drinking water as he would buy milk, at so much per gallon. You must not turn water out unless you can furnish other water. So, as a preliminary step, unless you are in a very great hurry, you should arrange to supply him with fresh water. That being done, I think you have a right to turn the water out of cisterns and pots. Otherwise people "won't stand for it," to use a slang expression.

The next general method for the elimination of yellow fever is the control of the human host. I told you, I think, that I regarded this as of small value where yellow fever is endemic and the people do not care. If I had a town like Guayaquil, for instance, I would not isolate a single man; I would not fumigate a single room; I would not go to the trouble of putting my finger on an infected mosquito, except for the purpose, maybe, of protecting a little foreign colony that might be in the place. I do not think any attempt from the human end would have any effect upon the time, by one day, when you would eliminate the fever. I would make my attempt entirely from the end of the insect. But it is very different in a town where yellow fever is not endemic. If this place be small, or if only a part of it be infected, and if you can have the cooperation of the people, as a rule you should make this the main attack, because it is possible to eliminate the fever in this way; and if so, you can do it much more quickly than by war on the mosquito. Even if you can not eliminate it you can always control it. And in those countries where it is not endemic frost will come after a while, and if you can keep it under control, lessen the rapidity of its spread, you can lessen the number of cases that will occur before frost stops it to a small proportion of what would have occurred had not these measures been taken.

In such a place, of course, there is no reason why you should not work from both ends, as White did in New Orleans and Gorgas in

Habana and Panama. I think I said all this yesterday, but the matter is so important that I repeat it.

I spoke of the cooperation of the people as being necessary for this work, and it is. You must work with the people; you must have their assistance if you hope to accomplish anything. You can not do efficient work if your activities are opposed by the community. I have tried it both ways and know.

Of course this method consists in finding the sick men, isolating them from mosquitoes, and destroying such mosquitoes as have had a chance to feed upon them before they were isolated. It hinges upon finding the sick man. If you can locate the disease and screen out the mosquitoes it is easy to destroy the mosquitoes that may have found access before you got there; but finding the sick man is not easy. You may have no difficulty in finding the bad cases, the cases that are known to be yellow fever. You have to bend every energy, and no trouble is too great, no precaution too trivial, to find the slightly sick man. By taking great pains in your search and by enlisting the support of the people, and through the laws and ordinances, you will find a great many.

The first thing to do is to lay out in your own mind the great fact that every man sick in a place where there is yellow fever is, from a sanitary standpoint, sick of yellow fever until the contrary is proved. I do not mean that every sick person actually has yellow fever. If, for instance, a man is reported as sick and you find he has a broken leg, you will know that his trouble is not yellow fever; but if you do not know that his leg is broken you had better look into his case and satisfy yourself just what the trouble is. And until you do know that the sick man has a broken leg he should be regarded as a case of yellow fever.

Sometimes you will find cases in which you can not tell whether they have yellow fever or something else. At McHenry, a little place in Mississippi, an epidemic broke out. It was a small place, but it was in June, and it was a place from which yellow fever could spread—a spark which could kindle a conflagration—and unusual precautions were justified. The town was divided into sections and every soul in it was seen twice a day. If any man was found sick he was seen by a physician and, unless the case was plainly not yellow fever, he was isolated. If anyone became sick at night or between visits in the day he was instructed to call a physician at once, and generally he did. In this way we kept a very close watch on the people in town and saw almost every case of sickness as soon as it occurred. To encourage the reporting of sickness not only was the family of the sick man put to no expense by his sickness; it and he were given all the help we could possibly manage. It was made an advantage to be sick, so as to get the sickness reported. Quite fre-

quently we were unable to say when we first saw a patient whether he had yellow fever or not, and we did isolate quite a number who did not have yellow fever, yet I think we isolated all who did have yellow fever. It was very close work and under good conditions for success—a small place, with fair cooperation of the people and a condition which required unusual effort. It was successful and the first suppression of an epidemic of yellow fever in the South in the summer of which I know.

In Panama we had laws compelling the reporting of cases of sickness and we had physicians whose duty it was to see everybody who was reported sick; and, finally, we made a tabulated list of every one in town who was susceptible to yellow fever—the "nonimmunes"—and had each one of them inspected daily. Anyone missing had to be accounted for by his lodging-house keeper, and anyone even suspected of being sick was seen by a physician. The detail was as well worked out and as well carried out as we could do it. The town, however, was fairly large and some part of the susceptible people were opposed to our efforts—not actively, but opposed all the same. We did not find all of the sick, or enough of them to get rid of the fever.

I tell you these things merely as illustrations. I can not tell you how to go about finding sick men. That is a thing that has to be left to yourself, as conditions vary. You must use your own judgment and all the ingenuity you have, and, as I said before, you must regard every sick person as having yellow fever until the contrary is proved. At McHenry we had free medicine and attendance. We furnished these and some delicacies to everyone who was sick, and when you do this you will be surprised to find out how many report sick. If you make it hard for them you will never find them. To be sick must be made a privilege. Having found them, they should be removed to a hospital and screened, or screened in their own houses. It is better to take them to hospital if they are willing to go, but it is better to screen them at home if the knowledge that they will be taken to hospital will prevent your finding other sick people. It is better to find 90 per cent of the sick people and screen them in their houses than to find 50 per cent and screen them in the hospital; and it may be a question between isolating them in their houses or not at all. The killing of mosquitoes is a very easy thing; the finding of all the sick men is a very hard problem.

That, I think, is all that I am going to say about the sanitation of yellow fever. The principles I have tried to give you and some of the details. The others you will work out for yourselves according to the nature of your problem. And remember that each officer of this service always improves on his predecessor.

The clinical aspects of yellow fever I do not purpose going into, but the diagnosis of the fever, especially its differential diagnosis, is a necessary point in the sanitarian's knowledge.

In the matter of diagnosis it is not worth while to say anything about the bad cases, the cases that anybody can tell. The cases that will give you trouble are the light cases and cases in the early stages. Early diagnosis is especially desirable. Therefore it is the clinical history of the light cases and of those in their early stages that I am going to try to give you.

In the first place, some cases are not diagnosable; you can not diagnosticate them. Here is a family—the mother, the father, two older girls, 16 and 13, possibly a boy of 12, and some children of 5 or 6 and younger—all sick. The adults plainly have yellow fever, and some of the children's cases can be diagnosticated as such, but some of the little children are simply sick of a light fever for a few days with no distinctive marks. It is reasonable to believe that all have the same disease, but some of them taken by themselves could not have been diagnosticated.

Yellow fever commences just like any other fever. You have pains and malaise; may have a chill and again you may not. About half the attacks commence at night. There is a feeling among southern physicians that nearly all attacks of yellow fever commence at night. I think not. A little more than half the attacks commence at night, and as few malarial chills come on at night, a chill that comes at night does help to exclude malaria. The pains and malaise are greater than you would expect from the elevation of temperature. When you find a man with a temperature of 102° and sick enough for 104° it is suspicious of yellow fever. It is so with some other diseases—dengue and plague, for example. Headache is almost invariable. I have seen only one patient that said at the time he had no headache. It is generally severe. Pains may be moderate and the degree is not of much prognostic import. I think I had the worst pains I ever saw in a case in the beginning, and I did not have a very bad case. Nausea and vomiting are rather more common than in the onset of other fevers. Constipation is almost invariable, but the bowels are not hard to move. Insomnia, or very troubled sleep, in the beginning is, in my experience, universal. The patient is restless and uncomfortable, more so than his temperature would lead you to expect. There is no albuminuria in the beginning. A slight leucocytosis; otherwise there is nothing to note in the blood picture.

His facies in the very beginning is extremely characteristic, I do not say "differential." It is not worth while to remember the "staring eyes" and all that is put in the books about it. Just remember that the first effect of yellow fever is to make an intense active capil-

lary congestion of the skin and mucous membranes. The eye will, of course, be bloodshot; on account of the active congestion it will be watery. The upper lip will be puffed and swollen. The whole face will be slightly puffed and red; the gums red; the tongue red; fauces red. It is simply the effect of an acute active congestion.

One thing about the conjunctivæ: Guiteras, who is a most acute diagnostician, says that the conjunctivæ on the first day show yellow. But about 95 per cent of the men I have seen in the South have yellow conjunctivæ without yellow fever. An examination of all the white male patients in Ancon Hospital once gave practically 100 per cent with yellow conjunctivæ.

About the third day the "stage of stasis" comes on. This is the "stage of calm" of the old books, only the "calm" does not always occur. Dutrolau says it may be so short as scarcely to be observable, which I judge is about the same thing. Calm does not always occur, but *stasis* is invariable. The whole aspect changes. In light cases and those of moderate severity—it is only of those I am speaking—the pains disappear; the distress and restlessness are gone. The patient can sleep now or rest without sleeping. His appearance changes absolutely and is now not only characteristic, but distinctive. He lies flat in bed on his back; slides down on his pillow. The whole appearance of the man as he lies in bed is one of rest. His mind is clear; he speaks only when it is necessary to speak; speaks slowly, distinctly with a low voice; and he is tired, very, very, tired. I know of a case of moderate severity where the man had an electric bell lashed to his hand and when he wanted anything all he had to do was to press a button with his thumb, but he would wait until he almost perished of thirst before he was willing to undertake the muscular exertion of pressing the button. The nurse would come in and ask him what he wanted and he would say "water;" not another word. It was even too much exertion for him to say "drink," which was perceptibly more laborious to pronounce. That is how tired he was.

The appearance of the face changes. The active congestion of skin and mucous membranes of the first stage is replaced by a passive congestion—a stasis. The face is no longer swollen; it is not bright red; shows a dusky pallor rather; the conjunctivæ are red, but with tortuous veins; they are dry rather than moist, making the "dull-red eye" of this stage. A distinct yellow color is nearly always observable in the eyes. The gums are red, but dark red and spongy and are apt to bleed spontaneously or on slight pressure. The facies (the appearance of the patient) is now not only characteristic, but distinctive. At this stage the diagnosis can quite frequently be made from the facies alone. It can always be suspected.

If one presses the finger on the chest or draws the nail along the skin the white mark made will be obliterated very slowly, and after finally turning red will remain so for some time. The mark is not white, by the way, but yellowish. This is the "tache" of the books, and simply means a sluggish circulation and some jaundice. The stomach is frequently painful; always tender. It is very painful in severe cases and tender enough in cases of moderate severity, requiring a cradle to keep off the pressure of the bedclothes. Having elicited tenderness, be satisfied and do not press on the stomach any more. This may produce vomiting.

Nausea, absent since the onset, may now return and is very apt to do so if food be taken. This, indeed, will likely lead to vomiting. Vomiting now if it occurs is a far graver symptom than that which came on with the attack. It is in this stage that gastric and intestinal hemorrhages occur, if they do occur.

Albuminuria is generally found on the evening of the third day. If it does not come on by the fourth day it is rarely found later.

Cases of moderate severity or a light case now proceed to get well, slowly at first. They are very weak at first. In a little while they will gain, and when they begin to improve they will gain as rapidly as in any disease I ever saw, and will get completely well so far as I know. They may turn markedly yellow in convalescence—eyes and skin—or they may not, more often in convalescence than during the sickness. There is no constant relation between the gravity of the disease and this sympton, but grave cases are nearly always yellow. There is always, I think, some yellowness.

I have never seen any ill effects after yellow fever. Patients either die from it at the time they have the disease or completely recover. I never saw any sequellæ of yellow fever, although Carroll is reported to have developed septic endocarditis from his yellow fever. I have known two physicians who believed they were permanently injured by it. Purnell died in 1909 of Bright's disease, which he thought was contracted from yellow fever in 1879. I doubt its origin. It lasted a long time. Dr. Burr contracted the fever in the epidemic of 1868 at New Orleans, which he was sure would shorten his life. He died in the spring of 1909, 73 years old. I doubt that yellow fever had very much to do with his death.

In yellow fever there are three signs which merit fuller exposition: Albuminuria, pulse and temperature, and hemorrhage.

First, albuminuria. In the beginning the urine is like the urine of any other fever, high colored and rather scanty, but on the second or third day albumen appears. Of course, you have albumen in almost any fever if you have fever enough, the agent causing the temperature reaction causing the albuminuria. But there are two

points in the albuminuria of yellow fever which are of note. In the first place, it comes with very little fever and it *is out of all proportion to the fever.* When you find a man with a temperature of 100° or 100.5°, with a fair amount of albuminuria and fever lasting not over three days, you suspect yellow fever. When you find a man with a temperature of 101.5° to 102°, with albumen that you have to shake out of the tube, that is not the ordinary albumen of high temperature of an ordinary infection.

The second and more important point is that the albumen *increases with the fall of fever.* In the cases I am talking of the fever reaches its maximum in 48 hours. It will possibly run three days and commence to fall, and the albumen in these cases shows usually on the third day and increases on the fourth and fifth days. I found a case on the fifth day with a temperature of 101°, and the albumen had to be shaken out of the test tube. That class of albumen is characteristic and differential. That is the albuminuria of yellow fever.

The early appearance of albumen is a bad prognostic. When it appears on the first day it goes to a fatal termination; on the second day it is of very bad augury. Also, let me caution you to examine the urine when you first see your patient. Albumen is not caused by yellow fever in the beginning, but your patient may have albuminuria from other causes, and it is important to know whether he has or not. To find albuminuria on the third day and to have a doubt raised if it were not there before the present sickness is annoying; while to find it absent at first and then present in considerable quantities as the fever declines is of diagnostic importance.

Since, in spite of the severity of the nephropathy, permanent lesions of the kidneys are rarely, if ever, left, it is evident that the toxin of this disease must especially attack the tubular epithelium. I have never seen blood macroscopically in the urine of yellow fever.

*Pulse and temperature.*—Yellow fever is not a disease of high temperatures. Rarely does it go over 103.5° even in bad cases. The temperature of light cases is highest on the first day. The temperature of moderate cases is highest on the first or second day, and then commences to fall; 100° to 102.5° would include, I suppose, nine-tenths of all cases of yellow fever we get in this country. The temperature is a continuous one. You can not, by the temperature, tell when the stage of stasis comes on. From the symptoms the advent of this stage marks a crisis in the disease, but there is no crisis in the temperature chart. The temperature goes on gradually down to the fourth or fifth day or a little beyond the sixth day. Bad cases have it somewhat longer, and some cases go on for three or four weeks; but that is not yellow fever; it is some complication. We try to explain it,

calling it "fever of secondary infection," which is as good a name as any other.

The pulse in the beginning is higher in proportion than it should be for the temperature. If you draw the pulse and temperature curves the pulse at first will probably run 10 to 20 beats more than it should for the temperature indicated. It then commences to drop. In most cases from the very beginning. The part of the abscissa included between the pulse and temperature curves increases as you go on. That is "Faget's sign." It is not always present, varying a good deal in different epidemics. It is, I think, less common in severe fevers. It was conspicuous by its absence—or rather rarity—in Panama. In Cuba it probably occurred in half the cases; in New Orleans it was much more common. Though not differential, it is a thing to look for. But you are quite apt to find the pulse falling away from the temperature in yellow fever. The lower the pulse within reason the better. I remember one man who had been quite sick and in convalescence I counted his pulse and found it 91 in three minutes, just about 30 to the minute, and he was doing very well.

Hemorrhagic signs usually appear first at the gums, for men at any rate. Examine the gums as soon as you see your patient. If the fever has just begun the gums, although bright red, will be of normal consistency. On the third or fourth day and later they should be soft, spongy, and bleeding on light pressure, or even spontaneously. Unless you examine them the first day you will not know the normal condition of the gums and could not then judge of the change that takes place in them, and it is this change you wish to know. Do not press the gums with the finger, or even with a handkerchief on the finger. This may cause gums which bleed easily—some people's do—to bleed independently of yellow fever. Press your finger lightly over the upper lip. Rarely will enough pressure be thus exerted to make the gums of a person in health bleed. Wipe it off the gums with a clean handkerchief. I am sorry to say that frequently you can not take the statement of your patient, or even of her physician, on the previous state of her gums if the fact that they are now bleeding is a point in the diagnosis of yellow fever. Hence, examine the gums as soon as you see her. Women and even female children well under puberty bleed from the genitalia. This for those over puberty is, I think, invariable. Capillary hemorrhages into the stomach and duodenum may occur during the stage of stasis and be shown either by the "black-vomit," beginning as small black or brown specks in the vomit, or as a tarry stool. The cases in which hemorrhages are a marked feature I need not describe; the laity will make your diagnosis.

The differential diagnosis should be plain to you from what I have said. What cases are you apt to mistake it for? Well, I have seen

typhoid fever mistaken for it, but that was not necessary. I have seen it mistaken for sunstroke. But you may, I think, legitimately mistake it for malarial fever, dengue, influenza, and measles. You will laugh at the last one as one of the things it is apt to be mistaken for.

*Malarial fever.*—The differential for malaria is, as a rule, fairly easy. Only do not lay too much stress on the plasmodia. If you do not find any plasmodia and the patient has not taken quinine, negatively the sign is of great value. Finding the plasmodium does not exclude yellow fever. Those of you who have been South will remember the outbreak of 1897 in Ocean Springs, where, because plasmodia were found in yellow fever cases, the diagnosis made was erroneous. We found malarial parasites in a large per cent of yellow fever cases from Cabanas, near Habana. They were not rare on the Isthmus. So the positive value of plasmodium is not of so much importance.

The time of onset is of some value. If the chill comes on in the night it is pretty certain not to be malaria, but if it comes in the daytime it does not exclude yellow fever.

The facies is distinct from malaria. A man would be unwise to make a diagnosis on the facies in the first stage, although he ought to be able to say that it was not malarial fever, and if malarial fever were the only alternative he would certainly be suspicious of yellow fever and count it yellow fever from a sanitary aspect.

The first year I was in Habana Maj. Gorgas and I used to go over to Cabanas early every morning to look over the sick people in the barracks there, and we used to write out the diagnoses of the men as we saw them. We saw, then, in the morning those who sickened in the night, within the first 12 hours of illness, so practically our guide was the facies. We were mistaken quite often, but rarely between yellow fever and malarial fever. Malarial fever plus alcoholism was less easy to differentiate from yellow fever.

*Dengue.*—Fortunately we can now tell dengue from yellow fever, and in the very beginning. It used to be very difficult, sometimes impossible, to tell one from the other in the early stages, and we had to wait. But the blood picture is absolutely characteristic, absolutely differential. Yellow fever gives a slight leucocytosis; dengue a profound leucopenia. It has been known to show as low as 2,500 leucocytes. I think in no other way can we be at all sure of differentiating between the two diseases in isolated cases in the beginning. Many people have written on the difficulty of telling the difference between the facies of yellow fever and the facies of dengue in the first stage of each, and each one has given his own minute and different points of distinction. There is *no* difference. The immediate underlying cause of the peculiar facies of the first stage—active capillary congestion—is the same for both, and naturally they both

present the same appearance. When it comes to the second stage it is different. The facies, then, is sufficient for the differential diagnosis, but we want to make the diagnosis early, and the blood picture is the differential between dengue and yellow fever or between dengue and any other acute disease I can think of.

*Influenza.*—When catarrhal symptoms are absent it is sometimes not very easy to tell influenza from yellow fever. I do not know how you can do this except to wait for the second stage. We had one case in Ancon Hospital that we held up until albumen appeared and found it was yellow fever. We had another case that we held up and waited till the albumen did not appear and found it was influenza.

*Measles.*—In the beginning this disease is very like yellow fever. One of the most acute diagnosticians I know of picked out a number of men from a regiment at Siboney as yellow fever cases that broke out with measles three days later. The facies misled him, and I have no doubt that anyone else not thinking of measles among grown men might have fallen into the same mistake. Knowing the possibility of this error, Koplik's spots should save us even if we did not wait for developments. I mention measles simply that you may suspect measles.

Let me give you one last point in diagnosis: If you do not know whether it is yellow fever or not—wait. You will know to-morrow or next day. Grave and damaging errors have I seen made by pronouncing a diagnosis when one did not know. It is a great pity not to be able to diagnose it in the first stage. But you had better not do it until the fourth day than diagnose wrongly. It is sometimes a serious thing to diagnose a case of dengue as yellow fever and still worse to say that yellow fever is dengue.

I wish I had time to tell you a little of pathological appearances and the diagnosis from autopsy, which is at times not only important but doubtful. I have not. I thank you for your attention.

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